Claims:

1. A combinatorial library of indolinone compounds, comprising at least ten indolinones that can be formed by reacting oxindoles with aldehydes.

2. The combinatorial library of claim 1 wherein said oxindoles are type A oxindoles.

3. The combinatorial library of claim 1 wherein said aldehydes are type B aldehydes.

4. A method of making an indolinone comprising the steps of

(a) creating a combinatorial library of indolinones by reacting a series of oxindoles with a series of aldehydes,

(b) testing said indolinones in biological assays,

(c) selecting one or more indolinones with favorable activity; and

(d) synthesizing one or more of said indolinones selected in step (c).

5. A 3-[(indole-3-yl)methylene]-2-indolinone compound having a substituent at the 1' position of the indole, where the substituent at the 1' position is selected from the group consisting of,

(a) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, aldehyde, or trihalomethyl substituents;

(b) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is

optionally substituted with one or more halogen or trihalomethyl substituents;

(c) an aldehyde or ketone of formula $-CO-R_{12}$, where $R_{12}$ is selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

(d) a carboxylic acid of formula $-(R_{13})_n-COOH$ or ester of formula $-(R_{14})_m-COO-R_{15}$, where $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;

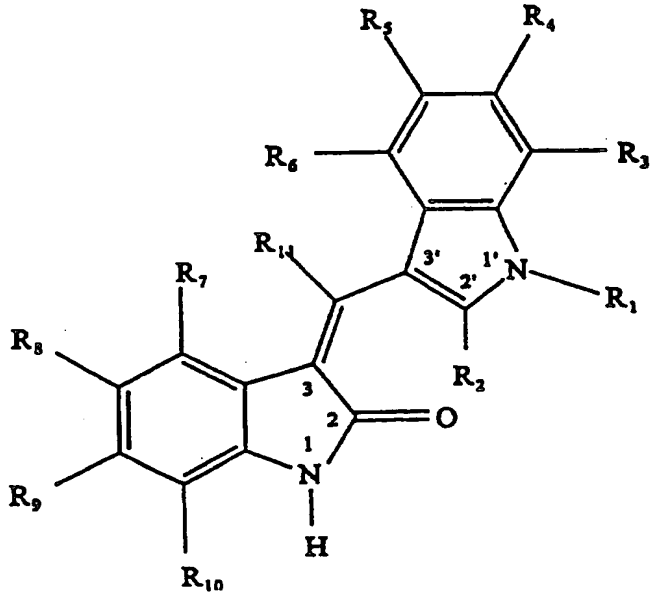
(e) a sulfone of formula $-(SO_2)-R_{16}$, where $R_{16}$ is selected from the group consisting of alkyl and a five or six membered heterocyclic ring, where the ring is optionally substituted with an alkyl moiety;

(f) $-(R_{17})_n-$(indole-1-yl) or

$-(R_{18})_m-CHOH-(R_{19})_p-$(indole-1-yl), where the indole moiety is optionally substituted with an aldehyde and $R_{17}$, $R_{18}$, and $R_{19}$ are alkyl and m, n, and p are independently 0 or 1; and

(g) taken together with a 2′ substituent of the indole ring forms a tricyclic moiety, where each ring in the tricyclic moiety is a five or six membered heterocyclic ring.

6. The compound, salt, isomer, metabolite, ester, amide, or prodrug of claim 5, wherein said compound has the formula,




where (a) $R_1$ is selected from the group consisting of,

(i) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, aldehyde, or trihalomethyl substituents;

(ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(iii) an aldehyde or ketone of formula -CO-$R_{12}$, where $R_{12}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(iv) a carboxylic acid of formula $-(R_{13})_n-COOH$ or ester of formula $-(R_{14})_m-COO-R_{15}$, where $R_{13}$, $R_{14}$, and $R_{15}$ and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and n and m are independently 0 or 1;

(v) a sulfone of formula $-(SO_2)-R_{16}$, where $R_{16}$ is selected from the group consisting of alkyl or a five or six membered heterocyclic ring, where the ring is optionally substituted with an alkyl moiety;

(vi) $-(R_{17})_n-$(indole-1-yl) or

$-(R_{18})_m-CHOH-(R_{19})_p-$(indole-1-yl), where the indole moiety is optionally substituted with an aldehyde and $R_{17}$, $R_{18}$, and $R_{19}$ are alkyl and n, m, and p are independently 0 or 1;

(vii) taken together with a 2' substituent of the indole ring forms a tricyclic moiety, where each ring in the tricyclic moiety is a five or six membered heterocyclic ring;

(b) $R_2$, $R_3$, $R_4$, $R_5$, and $R_6$ are selected from the group consisting of,

(i) hydrogen or alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, aldehyde, or trihalomethyl substituents;

(ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(iii) an aldehyde or ketone of formula

-CO-$R_{20}$, where $R_{20}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(iv) a carboxylic acid of formula -$(R_{21})_n$-COOH or ester of formula -$(R_{22})_m$-COO-$R_{23}$, where $R_{21}$, $R_{22}$, and $R_{23}$ and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(v) halogen or an alcohol of formula -$(R_{24})_m$-OH or an ether of formula -$(R_{24})_n$-O-$R_{25}$, where $R_{24}$ and $R_{25}$ are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(vi) -$NR_{26}R_{27}$, where $R_{26}$ and $R_{27}$ are independently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring; or -$NHCOR_{28}$, where $R_{28}$ is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

(vii) -$SO_2NR_{29}R_{30}$, where $R_{29}$ and $R_{30}$ are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;

(viii) any two of $R_3$, $R_4$, $R_5$, or $R_6$ taken together form a bicyclic or tricyclic heterocyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring;

(c) $R_7$, $R_8$, $R_9$, and $R_{10}$ are independently selected from the group consisting of,

(i) hydrogen or alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight,

nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, aldehyde, or trihalomethyl substituents;

(ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(iii) an aldehyde or ketone of formula

$-CO-R_{31}$, where $R_{31}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(iv) a carboxylic acid of formula $-(R_{32})_n-COOH$ or ester of formula $-(R_{33})_m-COO-R_{34}$, where $R_{32}$, $R_{33}$, and $R_{34}$ and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and n and m are independently 0 or 1;

(v) halogen or an alcohol of formula $-(R_{35})_m-OH$ or an ether of formula $-(R_{35})_n-O-R_{36}$, where $R_{35}$ and $R_{36}$ are independently chosen from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(vi) $-NR_{37}R_{38}$, where $R_{37}$ and $R_{38}$ are independently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring; or $-NHCOR_{39}$, where $R_{39}$ is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

(vii) $-SO_2NR_{40}R_{41}$, where $R_{40}$ and $R_{41}$ are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;

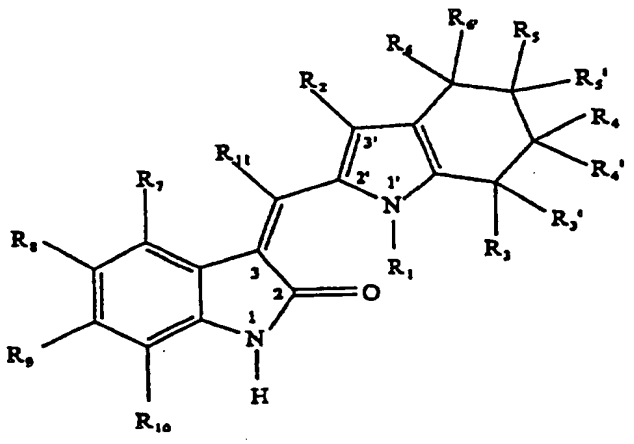
(viii) any two of $R_7$, $R_8$, $R_9$, or $R_{10}$ taken together form a bicyclic or tricyclic heterocyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring; and

(d) $R_{11}$ is hydrogen or alkyl; provided that at least one of $R_1$, $R_2$, $R_3$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$, $R_9$, or $R_{10}$ is alkyl or provided that at least four of $R_1$, $R_2$, $R_3$, $R_4$, $R_5$, or $R_6$ are not hydrogen.

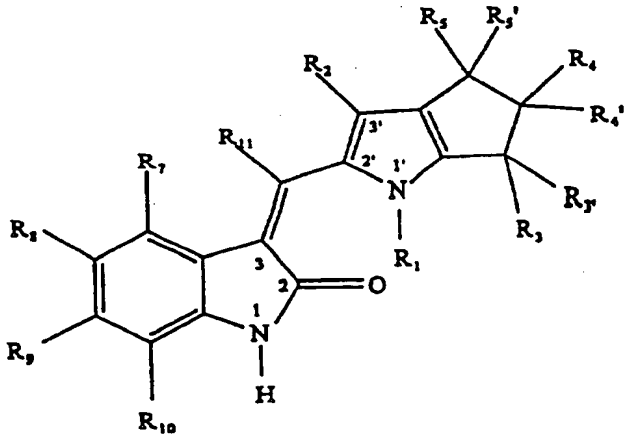
7. An optionally substituted 3-[(tetrahydroindole-2-yl)methylene]-2-indolinone or 3-[(cyclopentano-b-pyrrol-2-yl)methylene)-2-indolinone compound.

8. The indolinone compound of claim 7 of formula XIX or XX,

XIX



XX



or a pharmaceutically acceptable salt, isomer, metabolite, ester, amide, or prodrug thereof

where (a) $R_1$ is selected from the group consisting of,

(i) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally

substituted with one or more halogen, or trihalomethyl substituents;

(ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(iii) ketone of formula $-CO-R_{12}$, where $R_{12}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(iv) a carboxylic acid of formula $-(R_{13})_n-COOH$ or ester of formula $-(R_{14})_m-COO-R_{15}$, where $R_{13}$, $R_{14}$, and $R_{15}$ and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and n and m are independently 0 or 1;

(v) a sulfone of formula $-(SO_2)-R_{16}$, where $R_{16}$ is selected from the group consisting of alkyl or a five or six membered heterocyclic ring, where the ring is optionally substituted with an alkyl moiety;

(vi) $-(R_{17})_n-$(indole-1-yl) or

$-(R_{18})_m-CHOH-(R_{19})_p-$(indole-1-yl), where the indole moiety is optionally substituted with an aldehyde and $R_{17}$, $R_{18}$, and $R_{19}$ are alkyl and n, m, and p are independently 0 or 1;

(vii) taken together with a 2′ substituent of the indole ring forms a tricyclic moiety, where each ring in the tricyclic moiety is a five or six membered heterocyclic ring;

(b) $R_2$, $R_3$, $R_3'$, $R_4$, $R_4'$, $R_5$, $R_5'$, $R_6$ and $R_6'$ are selected from the group consisting of,

(i) hydrogen;

(ii) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;

(iii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(iv) ketone of formula $-CO-R_{20}$, where $R_{20}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(v) a carboxylic acid of formula $-(R_{21})_n-COOH$ or ester of formula $-(R_{22})_m-COO-R_{23}$, where $R_{21}$, $R_{22}$, and $R_{23}$ and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(vi) halogen;

(vii) an alcohol of formula $-(R_{24})_m-OH$ or an ether of formula $-(R_{24})_n-O-R_{25}$, where $R_{24}$ and $R_{25}$ are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(viii) $-NR_{26}R_{27}$, where $R_{26}$ and $R_{27}$ are independently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;

(ix) $-NHCOR_{28}$, where $R_{28}$ is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

(x) $-SO_2NR_{29}R_{30}$, where $R_{29}$ and $R_{30}$ are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;

(xi) any two of $R_3$, $R_3'$, $R_4$, $R_4'$, $R_5$, $R_5'$, $R_6$, or $R_6'$ taken together form a bicyclic or tricyclic heterocyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring;

(c) $R_7$, $R_8$, $R_9$, and $R_{10}$ are independently selected from the group consisting of,

(i) hydrogen;

(ii) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;

(iii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(iv) ketone of formula $-CO-R_{31}$, where $R_{31}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(v) a carboxylic acid of formula $-(R_{32})_n-COOH$ or ester of formula $-(R_{33})_m-COO-R_{34}$, where $R_{32}$, $R_{33}$, and $R_{34}$ are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and n and m are independently 0 or 1;

(vi) halogen;

(vii) an alcohol of formula $-(R_{35})_m-OH$ or an ether of formula $-(R_{35})_n-O-R_{36}$, where $R_{35}$ and $R_{36}$ are

independently chosen from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(viii) $-NR_{37}R_{38}$, where $R_{37}$ and $R_{38}$ are independently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;

(ix) $-NHCOR_{39}$, where $R_{39}$ is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

(x) $-SO_2NR_{40}R_{41}$, where $R_{40}$ and $R_{41}$ are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;

(xi) any two of $R_7$, $R_8$, $R_9$, or $R_{10}$ taken together form a bicyclic or tricyclic heterocyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring; and

(d) $R_{11}$ is hydrogen or alkyl

9. An indolinone compound having a substituent at the 5 position of the oxindole ring, where the substituent at the 5 position of the oxindole ring is selected from the group consisting of

(a) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;

(b) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(c) a ketone of formula $-CO-R_{10}$, where $R_{10}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(d) a carboxylic acid of formula $-(R_{11})_n-COOH$ or ester of formula $-(R_{12})_m-COO-R_{13}$, where $R_{11}$, $R_{12}$, and $R_{13}$ and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(e) halogen;

(f) an alcohol of formula $-(R_{14})_m-OH$ or an ether of formula $-(R_{14})_n-O-R_{15}$, where $R_{14}$ and $R_{15}$ are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;

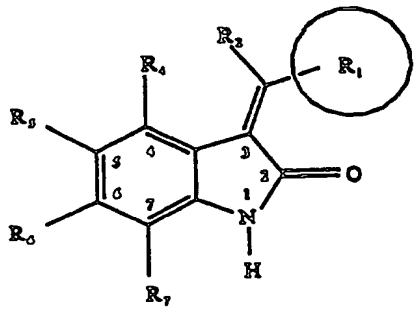
(g) $-NR_{16}R_{17}$, where $R_{16}$ and $R_{17}$ are independently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

(h) $-NHCOR_{18}$, where $R_{18}$ is selected from the group consisting of alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

(i) $-SO_2NR_{19}R_{20}$, where $R_{19}$ and $R_{20}$ are selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

(j) any two of $R_4$, $R_5$, $R_6$, or $R_7$ taken together form a bicyclic or tricyclic heterocyclic moiety fused to the six membered ring of the oxindole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring.

10. The compound of claim 9 of the following formula,




where (a) $R_5$ is selected from the group consisting of,

(i) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;

(ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(iii) a ketone of formula $-CO-R_{10}$, where $R_{10}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(iv) a carboxylic acid of formula $-(R_{11})_n-COOH$ or ester of formula $-(R_{12})_m-COO-R_{13}$, where $R_{11}$, $R_{12}$, and $R_{13}$ and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(v) halogen;

(vi) an alcohol of formula $-(R_{14})_m-OH$ or an ether of formula $-(R_{14})_n-O-R_{15}$, where $R_{14}$ and $R_{15}$ are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(vii) $-NR_{16}R_{17}$, where $R_{16}$ and $R_{17}$ are independently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

(viii) $-NHCOR_{18}$, where $R_{18}$ is selected from the group consisting of alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

(ix) $-SO_2NR_{19}R_{20}$, where $R_{19}$ and $R_{20}$ are selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

(x) any two of $R_4$, $R_5$, $R_6$, or $R_7$ taken together form a bicyclic or tricyclic heterocyclic moiety fused to the six membered ring of the oxindole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring;

(b) $R_1$ is selected from the group consisting of a five, six, eight, nine, and ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more substituents selected from the group consisting of

(i) hydrogen and alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;

(ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(iii) a ketone of formula $-CO-R_{21}$, where $R_{21}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(iv) a carboxylic acid of formula $-(R_{22})_n-COOH$ or ester of formula $-(R_{23})_m-COO-R_{24}$, where $R_{22}$, $R_{23}$, and $R_{24}$ and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(v) halogen;

(vi) an alcohol of formula $-(R_{25})_m-OH$ or an ether of formula $-(R_{25})_n-O-R_{26}$, where $R_{25}$ and $R_{26}$ are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(vii) $-NR_{27}R_{28}$, where $R_{27}$ and $R_{28}$ are independently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

(viii) $-NHCOR_{29}$, where $R_{29}$ is selected from the group consisting of alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

(ix) $-SO_2NR_{30}R_{31}$, where $R_{30}$ and $R_{31}$ are selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

(c) $R_4$, $R_6$, and $R_7$ are independently selected from the group consisting of,

(i) hydrogen and alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;

(ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;

(iii) a ketone of formula $-CO-R_{32}$, where $R_{32}$ is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

(iv) a carboxylic acid of formula $-(R_{33})_n-COOH$ or ester of formula $-(R_{34})_m-COO-R_{35}$, where $R_{33}$ $R_{34}$ and $R_{35}$ and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

(v) halogen;

(vi) an alcohol of formula $-(R_{36})_m-OH$ or an ether of formula $-(R_{36})_n-O-R_{37}$, where $R_{36}$ and $R_{37}$ are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;

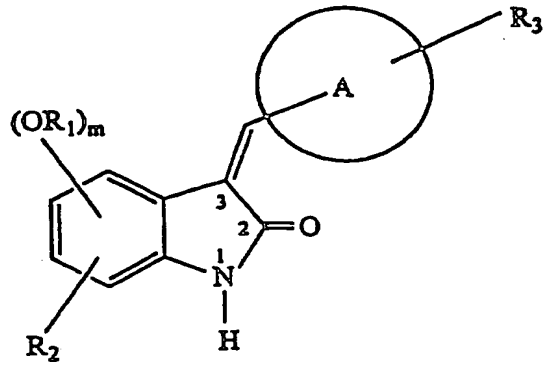
(vii) $-NR_{38}R_{39}$, where $R_{38}$ and $R_{39}$ are independently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

(viii) $-NHCOR_{40}$, where $R_{40}$ is selected from the group consisting of alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

(ix) $-SO_2NR_{41}R_{42}$, where $R_{41}$ and $R_{42}$ are selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring; and

(d) $R_2$ is hydrogen or alkyl.

11. A compound having formula XXI, wherein:




XXI

(a) A is a five or six membered ring comprised of atoms selected from the group consisting of oxygen, carbon, sulfur and nitrogen;

(b) m is zero, 1, or 2;

(c) $R_1$ is hydrogen, $C_1$-$C_6$ alkyl or $C_2$-$C_6$ alkanoyl;

(d) one of $R_2$ and $R_3$ independently is hydrogen and the other is a substituent selected from:

(1) a $C_1$-$C_6$ alkyl group substituted by 1, 2 or 3 hydroxy groups;

(2) $SO_3R_4$ in which $R_4$ is hydrogen or $C_1$-$C_6$ alkyl unsubstituted or substituted by 1, 2 or 3 hydroxy groups;

(3) $SO_2NHR_5$ in which $R_5$ is as $R_4$ defined above or a-$(CH_2)_n$-$N(C_1$-$C_6$ alkyl$)_2$ group in which n is 2 or 3;

(4) $COOR_6$ in which $R_6$ is $C_1$-$C_6$ alkyl unsubstituted or substituted by phenyl or by 1, 2 or 3 hydroxy groups or phenyl;

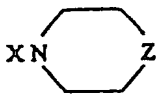
(5) $CONHR_7$, in which $R_7$ is hydrogen, phenyl or $C_1$-$C_6$ alkyl substituted by 1, 2 or 3 hydroxy groups or by phenyl;

(6) $NHSO_2R_8$ in which $R_8$ is $C_1$-$C_6$ alkyl or phenyl unsubstituted or substituted by halogen or by $C_1$-$C_4$ alkyl;

(7) $N(R_9)_2$, $NHR_9$ or $OR_9$ wherein $R_9$ is $C_2$-$C_6$ alkyl substituted by 1, 2 or 3 hydroxy groups;

(8) $NHCOR_{10}$, $OOCR_{10}$ or $CH_2OOCR_{10}$ in which $R_{10}$ is $C_1$-$C_6$ alkyl substituted by 1, 2 or 3 hydroxy groups;

(9) $NHCONH_2$; $NH$-$C(NH_2)$=$NH$; $C(NH_2)$=$NH$; $CH_2NHC(NH_2)$=$NH$; $CH_2NH_2$; $OPO(OH)_2$; $CH_2OPO(OH)_2$; $PO(OH)_2$; or a




wherein X is selected from the group consisting of $CH_2$, $SO_2$, CO, or $NHCO(CH_2)_p$ in which p is 1, 2, or 3 and Z is $CH_2$, O or N-$R_{11}$ in which $R_{11}$ is hydrogen or is as $R_9$ defined above.

12. A method of making an indolinone compound of any one of claims 5-11 comprising the steps of reaching an appropriate aldehyde and oxindole and separating the indolinone from the aldehyde and oxindole reactants.

13. A pharmaceutical composition comprising (i) a pharmaceutically acceptable carrier or excipient and (ii) a compound according to any one of claims 5-11.

14. A method for treating a disease related to unregulated tyrosine kinase signal transduction, the method comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound according to anyone of claims 5-11.

15. A method for regulating tyrosine kinase signal transduction comprising administering to a subject a therapeutically effective amount of a compound according to any one of claims 5-11.

16. A method of preventing or treating an abnormal condition in an organism, where the abnormal condition is associated with an aberration in a signal transduction pathway characterized by an interaction between a protein kinase and a natural binding partner, where the method comprises the following steps:

(a) administering a compound of any one-of claims 5-11 to an organism; and

(b) promoting or disrupting the abnormal interaction.

17. A method of preventing or treating an abnormal condition in an organism, where the abnormal condition is associated with an aberration in a signal transduction pathway characterized by an interaction between a protein kinase and a natural binding partner, where the method comprises the following steps:

(a) administering a compound of any one of claims 5-11 to an organism; and

(b) promoting or disrupting the abnormal interaction.